

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) An isolated peptide comprising the sequence
Trp₁-Glu₁-Val-Leu-Cys₁-Trp₂-Thr₁-Trp₃-Glu₂-Thr₂-Cys₂-Glu₃-Arg

(SEQ ID NO: 4),

wherein between zero and eight amino acids of SEQ ID NO: 4 are substituted according to the following:

Trp₁ is Trp, Phe, Tyr, Leu, Ile, Met, Val or Ala;

Glu₁ is any amino acid;

Val is Val, Trp, Phe, Tyr, Leu, Ile, Met or Ala;

Leu is Leu, Trp, Phe, Tyr, Ile, Met, Val or Ala;

Trp₂ is Trp, Phe, Tyr, Leu, Ile, Met, Val or Ala;

Thr₁ is any amino acid;

Trp₃ is Trp, Phe, or Tyr, ~~Leu, Ile, Met, Val or Ala;~~

Glu₂ is any amino acid;

Thr₂ is any amino acid;

Glu₃ is any amino acid;

Arg is Arg, Lys, Leu, Trp, His, Met or Ile; and wherein the peptide binds FVII/FVIIa in an *in vitro* assay.

2. (Currently Amended) The isolated peptide of claim 1,

wherein between zero and eight amino acids of SEQ ID NO: 4 are substituted according to the following:

Trp₁ is Trp, Phe or Leu;

Glu₁ is any amino acid;

Val is Val or Ile;

Leu is Leu, Ile, Met, Val or Ala;

Trp₂ is Trp, Phe, Tyr, Leu or Met;

Thr₁ is any amino acid;

Trp₃ is Trp;
Glu₂ is any amino acid;
Thr₂ is any amino acid;
Glu₃ is any amino acid;
Arg is Arg, Lys, Leu or Trp.

3. (Currently Amended) The isolated peptide of claim 2 having an IC₅₀ for FVII/FVIIa of less than 1 μM.
4. (Currently amended) The isolated peptide of claim 3 having an IC₅₀ for FVII/FVIIa of less than 100 nM.
5. (Currently amended) The isolated peptide of claim 4 having an IC₅₀ for FVII/FVIIa of less than 10 nM.
6. (Currently Amended) The isolated peptide of claim 1 which inhibits FVIIa activity.
7. (Currently amended) The isolated peptide of claim 6 which blocks an activity associated with FVIIa selected from the group consisting of activation of FVII, activation of FIX and activation of FX.
8. (Currently amended) The isolated peptide of claim 7 which inhibits activation of FX.
9. (Currently amended) The isolated peptide of claim 8 having an IC₅₀ for inhibiting FX activation of less than 10 μM.
10. (Currently amended) The isolated peptide of claim 9 having an IC₅₀ for inhibiting FX activation of less than 100 nM.
11. (Currently amended) The isolated peptide of claim 10 having an IC₅₀ for inhibiting FX activation of less than 5 nM.

12. (Currently Amended) The isolated peptide of claim 1, having the following formula:

$$X_i\text{-Trp}_1\text{-Glu}_1\text{-Val-Leu-Cys}_1\text{-Trp}_2\text{-Thr}_1\text{-Trp}_3\text{-Glu}_2\text{-Thr}_2\text{-Cys}_2\text{-Glu}_3\text{-Arg-X}_k$$
wherein X_i is absent or is between 1 and 100 amino acids; and X_k is absent or between 1 and 100 amino acids.

13. (Currently amended) The isolated peptide of claim 12 wherein X_i and X_k are between 1 and 50 amino acids.

14. (Currently amended) The isolated peptide of claim 13 wherein X_i and X_k are between 1 and 10 amino acids.

15. (Currently Amended) The isolated peptide of claim 14 having the formula

$$\text{Xaa}_1\text{-Xaa}_2\text{-Trp}_1\text{-Glu}_1\text{-Val-Leu-Cys}_1\text{-Trp}_2\text{-Thr}_1\text{-Trp}_3\text{-Glu}_2\text{-Thr}_2\text{-Cys}_2\text{-Glu}_3\text{-Arg-Xaa}_{16}\text{-Xaa}_{17}\text{-Xaa}_{18}$$
, wherein between zero and eight amino acids are substituted according to the following:
 - Xaa₁ is an amino acid;
 - Xaa₂ is an amino acid;
 - Trp₁ is Trp, Phe, Leu, Ala, Met or Val;
 - Glu₁ is an amino acid;
 - Val is Val, Ile, Ala, Trp or Tyr;
 - Leu is Leu, Ile, Met, Val or Ala;
 - Trp₂ is Trp, Phe, Leu, Met, Ala or Val;
 - Thr₁ is an amino acid ;
 - Trp₃ is Trp, Phe, Met or Tyr;
 - Glu₂ is an amino acid;
 - Thr₂ is an amino acid;
 - Glu₃ is an amino acid except proline;
 - Arg is Arg, Lys, Leu, Trp, His or Met;
 - Xaa₁₆ is an amino acid;
 - Xaa₁₇ is an amino acid; and

Xaa₁₈ is an amino acid.

16. (Currently Amended) The isolated peptide of claim 15, wherein
Trp₁ is Trp, Phe, Leu or Ala;
Val is Val, Ile or Ala; and
Trp₂ is Trp, Phe, Leu, Met or Ala.
17. (Currently Amended) The isolated peptide of claim 16, wherein
Trp₁ is Trp, Phe, or Leu;
Val is Val or Ile;
Leu is Leu, Ile, Met or Val;
Trp₂ is Trp, Phe, Leu or Met;
Trp₃ is Trp; and
Arg is Arg, Lys, Leu or Trp.
18. (Currently Amended) The isolated peptide of claim 17, wherein - Trp₂-Thr₁-Trp₃-Glu₂-Thr₂- is
-Trp-Thr-Trp-Glu-Thr- (SEQ ID NO:100).
19. (Withdrawn and Currently Amended) A method of inhibiting FVIIa activity comprising the step of:
 - a) contacting FVIIa with [[a]] the isolated peptide of claim 1 in the presence of tissue factor and under conditions which allow binding of the compound to FVIIa to occur.
20. (Withdrawn and Currently Amended) A method for selecting a compound which blocks FVII/FVIIa activation of FX comprising the steps of:
 - (1) contacting FVII/FVIIa with ~~a compound~~ the isolated peptide of claim 1 in the presence and absence of a candidate molecule under conditions which allow specific binding of the ~~compound~~ isolated peptide of claim 1 to FVII/FVIIa to occur;
 - (2) detecting the amount of specific binding of the ~~compound~~ isolated peptide of claim 1 to FVII/FVIIa that occurs in the presence and absence of the candidate compound

wherein the amount of binding in the presence of the candidate compound relative to the amount of binding in the absence of the candidate molecule is indicative of the ability of the candidate compound to block FVII/FVIIa activation of FX.

21. (Withdrawn and Currently Amended) A method of inhibiting the activation of FX comprising contacting FVII/FVIIa with a compound that prevents the interaction of FVII/FVIIa with ~~a compound~~ the isolated peptide of claim 1.

22. (Withdrawn and Currently Amended) The method of ~~inhibiting the activation of FX of~~ claim 21, ~~wherein the comprising contacting FVII/FVIIa with a compound that prevents the interaction of FVII/FVIIa with~~ the isolated peptide comprises SEQ ID NO: 4.

23. (Withdrawn) The method of claim 22, wherein the contacting occurs *in vivo*.

24. (Withdrawn) The method of claim 22, wherein the contacting occurs *in vitro*.

25. (Withdrawn and Currently Amended) A method of treating a TF/FVIIa mediated disease or disorder in a host in need thereof comprising administering to the host a therapeutically effective amount of ~~a compound~~ the isolated peptide of claim 1.

26. (Withdrawn and Currently Amended) A method of treating a TF/FVIIa mediated disease or disorder in a host in need thereof comprising administering to the host a therapeutically effective amount of the isolated peptide of claim 1.

27. (Cancelled)

28. (Currently Amended) A pharmaceutical composition comprising the isolated peptide of claim 1 and a pharmaceutically acceptable carrier.

29. (Original) The composition of claim 28, which is suitable for inhalation.

30. (Previously Presented) The composition of claim 29, which is dry powder.
31. (Previously Presented) The composition of claim 29, which is a liquid.
32. (Currently Amended) An isolated disulfide-constrained peptide comprising the formula
 Trp₁-Glu₁-Val-Leu-Cys₁-Trp₂-Thr₁-Trp₃-Glu₂-Thr₂-Cys₂-Xaa-Arg, wherein between zero
 and five amino acids are substituted according to the following:
 Leu is substituted with Met, Ile, or Val;
 Thr₁ is substituted with Ala, Ser, Glu, Gly, Asp, or Gln;
 Thr₂ is Gly, Asp, Gln, Ala, Ser, Glu, Thr, Val, or Asn;
 Xaa is any amino acid; and
 Arg is Leu, Ser or Trp.
33. (Currently Amended) The isolated disulfide-constrained peptide of claim 32, wherein the
 peptide comprises:
 Trp₁-Glu₁-Val-Leu-Cys₁-Trp₂-Thr₁-Trp₃-Glu₂-Thr₂-Cys₂-Xaa-Arg, wherein between zero
 and five amino acids are substituted according to the following:
 Leu is substituted with Met, Ile, or Val;
 Thr₁ is substituted with Ala, Ser, Glu, Gly, Asp, or Gln;
 Thr₂ is Gly, Asp, Gln, Ala, Ser, Glu, Thr, Val, or Asn; and
 Xaa is any amino acid.
34. (Currently Amended) The isolated disulfide-constrained peptide of claim 32, wherein the
 peptide comprises:
- | | |
|----------------------|--------------------------|
| SAEWEVLCWTWEGCGSVGLV | (SEQ ID NO:1) TF53; |
| SEWEVLCWTWEDCRLEGLE | (SEQ ID NO:2) TF57; |
| WEVLCWTWEDCER | (SEQ ID NO:3) TF 64; |
| WEVLCWTWETCER | (SEQ ID NO:4) TF 65; |
| WEVVCWTWETCER | (SEQ ID NO:5) TF 66; |
| EWEVLCWTWETCERGE | (SEQ ID NO:17) TF99; |
| EEWEVLCWTWETCEREGEG | (SEQ ID NO:18) TF100; or |

EEWEVLCWTWETCER (SEQ ID NO:23) TF183.

35. (Withdrawn and Currently Amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

SAEWEVLCWTWEGCGSVGLV (SEQ ID NO:1) TF53.

36. (Withdrawn and Currently Amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

SEEWEVLCWTWEDCRLEGL (SEQ ID NO:2) TF57.

37. (Withdrawn and Currently Amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

WEVLCWTWEDCER (SEQ ID NO:3) TF 64.

38. (Currently Amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

WEVLCWTWETCER (SEQ ID NO:4) TF65.

39. (Withdrawn and currently amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

WEVVCWTWETCER (SEQ ID NO:5) TF 66.

40. (Withdrawn and currently amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

EWEVLCWTWETCERGE (SEQ ID NO:17) TF99.

41. (Withdrawn and currently amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

EEWEVLCWTWETCER GEG (SEQ ID NO:18) TF100.

42. (Withdrawn and currently amended) The isolated disulfide-constrained peptide of claim 34, wherein the peptide comprises:

EEWEVLCWTWETCER

(SEQ ID NO:23) TF183.

43. (Currently Amended) The isolated peptide of claim 1, 12, or 32, wherein the N terminal amino acid is modified, the C terminal amino acid is modified, or both the N and C terminal amino acids are modified.

44. (New) The isolated peptide of claim 32, wherein the peptide is the N-terminal portion or the C terminal portion of a hybrid molecule.

45. (New) The isolated peptide of claim 44, wherein the hybrid molecule comprises the isolated peptide of claim 32 linked to one or more of a multimerization domain, linker domain, another protein domain, or another isolated peptide of claim 32.